



## Diabetes

## Dateline

National Diabetes Information Clearinghouse

Fall 2006

## Gene Variant Increases Type 2 Diabetes Risk

### Lifestyle Changes Can Trump Genetics

**H**aving a copy of a particular gene variant ups the risk of developing type 2 diabetes, a new study confirmed. But even study participants at highest genetic risk benefited from healthy lifestyle changes, such as increased physical activity and a nutritious diet, as much as—if not more than—those without that risk.

Researchers from the Diabetes Prevention Program (DPP) Genetics subgroup—a collaborative effort involving the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), Massachusetts General Hospital, George Washington University, and the University of Maryland—found one copy of the gene variant called *TCF7L2* in 40 percent of the DPP participants and two copies in 10 percent of participants.

For carriers of two copies of the gene variant, the risk of developing type 2 diabetes is about 80 percent higher than for noncarriers.

### Lifestyle Matters

Researchers found that lifestyle changes can have a big impact on type 2 diabetes. “The lifestyle intervention reduced risk even in those who carried both copies of the risk variant,” said lead study author Jose Florez, M.D., Ph.D., a staff endocrinologist at Massachusetts General Hospital in Boston. “This finding emphasizes that people at risk of diabetes, whether they’re overweight, have elevated blood glucose levels, or have this particular gene variant, can benefit greatly by implementing a healthy lifestyle.”



Building on the work of the biopharmaceutical company deCode Genetics that linked a gene variant and type 2 diabetes, the DPP Genetics subgroup

- confirmed the finding in an independent population that included the racial and ethnic diversity typical of the U.S. population with diabetes
- showed that the gene variant increased risk in those with pre-diabetes, and in those in a prospective study where patients are followed over time

**GENE VARIANT**, continued on page 2

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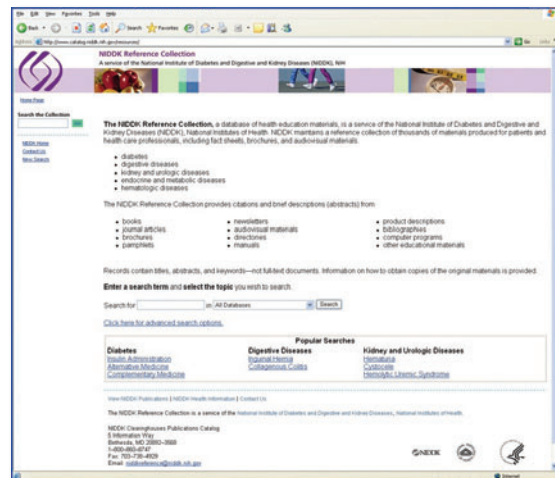
National Institute of  
Diabetes and Digestive  
and Kidney Diseases



## From the NIDDK Reference Collection

Looking for a hard-to-find resource on diabetes? Try using the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Reference Collection. This free, online, searchable database helps health care professionals, health educators, patients, and the general public find educational materials not typically referenced in most databases.

The NIDDK Reference Collection currently houses more than 8,000 summaries that include a resource's title, author(s), publisher, abstract, and keywords. Also included is information about how to get full-text copies of nonjournal resources such as foreign-language materials, books and book chapters, brochures, pamphlets, fact sheets, CD-ROMs, coloring books, bibliographies, audiovisual materials, posters, computer programs, government documents, product descriptions, newsletters, and manuals.



Visit <http://catalog.niddk.nih.gov/resources> to access the Reference Collection.

## NIDDK Reference Collection Spotlight

A recent addition to the Reference Collection is a diabetes microalbuminuria screening and management chart. The simple chart diagrams care management for people with diabetes who test positive for microalbuminuria, or microscopic protein in the urine. The chart walks health care providers through the recommended screening and monitoring tests for patients with the condition and includes notations for when to refer a patient to a nephrologist. The laminated card from the National Kidney Foundation uses different colors on the decision-making grid. ■

### GENE VARIANT, from page 1

- examined for the first time the relationship between the genetic risk factor and interventions that delay diabetes onset
- demonstrated that the gene variant affects insulin production, not cell response to insulin

Even though the gene link predicts a greater risk of developing type 2 diabetes, researchers do not recommend routine genetic testing.

The DPP, spearheaded by the NIDDK in 1995, was a major clinical trial aimed at discovering whether diet or exercise or both—or the oral diabetes drug metformin—could delay type 2 diabetes onset in people with impaired glucose tolerance. The program ended in 2001.

Visit [www.diabetes.niddk.nih.gov/dm/pubs/preventionprogram](http://www.diabetes.niddk.nih.gov/dm/pubs/preventionprogram) for more information about the DPP. ■

### Diabetes Dateline

*Diabetes Dateline*, an email newsletter, is sent to subscribers four times a year by the National Diabetes Information Clearinghouse (NDIC). The newsletter features news about diabetes, special events, patient and professional meetings, and new publications available from the NDIC and other organizations.

If you would like to subscribe, send an email to [niddk@info.niddk.nih.gov](mailto:niddk@info.niddk.nih.gov). You can read or download a PDF version of the newsletter at [www.diabetes.niddk.nih.gov/about/newsletter.htm](http://www.diabetes.niddk.nih.gov/about/newsletter.htm).



## Early Type 2 Diabetes Linked to Higher Kidney Failure, Mortality Risk

People who develop type 2 diabetes before age 20 have substantially higher rates of kidney failure and mortality by middle age than those who develop diabetes after age 20, according to a recent study by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

Researchers analyzed 37 years of data on a Southwestern American Indian tribe with an exceedingly high rate of type 2 diabetes. Among 1,856 participants with diabetes, 96 had developed the disease before age 20.

Researchers found that people with youth-onset diabetes were eight times more likely to have kidney failure, or end-stage renal disease (ESRD), between the ages of 25 and 34 than those diagnosed after age 20. The youth-onset group also was five times more likely to have kidney failure between the ages of 35 and 44 and four times more likely to have ESRD between the ages of 45 and 54 than those who developed diabetes later in life.



The age-sex-adjusted death rate in participants with youth-onset diabetes was more than twice as high as in those with older-onset diabetes.

The results of this study are significant for other populations “because we’re seeing more people in all ethnic groups developing type 2 diabetes in youth,” according to Robert G. Nelson, M.D., Ph.D., an NIDDK researcher. “Those developing diabetes in youth will be confronting the complications of diabetes in midlife. At a time when most people their age are caring for children and aging parents and saving for retirement and their children’s college education, many of those with youth-onset diabetes may be needing care themselves.”

The study, “Effect of Youth-Onset Type 2 Diabetes Mellitus on Incidence of End-Stage Renal Disease and Mortality in Young and Middle-Aged Pima Indians,” was published in the July 26, 2006, issue of the *Journal of the American Medical Association*. ■

## RBP4 Appears to Identify Insulin Resistance, Study Reveals

Findings from a recent study support the development of antidiabetic therapies aimed at lowering serum retinol-binding protein 4 (RBP4) levels. RBP4 is a protein secreted by fat cells and the liver that is elevated before clinically evident diabetes develops.

Researchers sought to determine whether serum RBP4 levels correlated with insulin resistance and changed after an intervention that improved insulin sensitivity. They found that serum RBP4 levels correlated with the magnitude of insulin resistance in patients with obesity, impaired glucose tolerance, or type 2 diabetes, and in nonobese, nondiabetic patients with a strong family history of type 2 diabetes.

Elevated serum RBP4 was associated with components of metabolic syndrome, including increased body mass index, waist-to-hip ratio, serum triglyceride levels, systolic blood pressure, and decreased high-density lipoprotein cholesterol levels.

Senior author Barbara Kahn and colleagues showed in a previous study that in mice, increasing serum RBP4 levels causes insulin resistance. “We do not yet know if RBP4 also causes insulin resistance in humans, but if it does, this will open up an entirely new mechanistic pathway underlying the pathogenesis of type 2 diabetes and the metabolic syndrome,” said Kahn, a professor of medicine at Harvard Medical School and chief of the division of endocrinology, diabetes, and metabolism at Beth Israel Deaconess Medical Center in Boston.

The study, “Retinol-binding Protein 4 and Insulin Resistance in Lean, Obese, and Diabetic Subjects,” was published in the June 15, 2006, issue of the *New England Journal of Medicine*. ■

## Trove of NIDDK Data, Samples Growing in Popularity

### Repository Makes Free Study Data Available to Researchers

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is seeing an upwelling of interest in its fledgling repositories of study data, particularly the resource giving investigators access to detailed information from the Diabetes Prevention Program (DPP) and other landmark NIDDK trials.

Data and biosamples from the following trials are now available:

- The Diabetes Prevention Program
- The Diabetes Prevention Type 1 Trial
- The NIDDK Liver Transplantation Database
- The National Analgesic Nephropathy Study
- The Modification of Diet in Renal Disease Study
- The Interstitial Cystitis Database

Go to [www.niddkrepository.org](http://www.niddkrepository.org) for more information.

The data are available through the NIDDK Central Repository at [www.niddkrepository.org](http://www.niddkrepository.org). By ensuring the information is easily and freely accessible, Rebekah Rasooly, Ph.D., who oversees the NIDDK project, said any researcher can generate hypotheses without spending months of time or millions of dollars.

“A certain amount of activation energy is needed to start new research. In the past, it has almost not been worth the effort,” she said, outlining the arduous process of contacting investigators and acquiring data. “With the Central Repository, it’s available to anyone, and it’s available in a very streamlined manner.”

### ‘Enormously Valuable’

Rasooly said she is especially excited by the prospect of additional analysis of the DPP findings. “The DPP is enormously valuable,” said Rasooly. “Its findings represent lynchpin data in what is a key public health study.”

The overall finding—that lifestyle changes can prevent or delay type 2 diabetes in high-risk individuals—has already helped alter the way doctors and patients approach the disease. The repository enables researchers to more carefully examine certain populations and further hone prevention messages.

In addition to raw data, the Central Repository archives DNA information and biological samples such as blood and tissue from certain NIDDK-funded studies. Data sets are available free of charge to requestors, though requests that require

the NIDDK to do more than 2 hours of analytical work are billed. Access to samples from the DNA and biosample repositories requires approval from a review panel.

### Expanding and Promoting

Rasooly said the NIDDK is “constantly expanding” the Central Repository, which is a key resource for maximizing the value of large, multisite, NIDDK-funded clinical trials by making as much data as possible available from those studies.

“The NIDDK has launched a number of large, multisite trials,” said Rasooly. “The repositories leverage the value of these studies.”

The NIDDK funds a biosample repository, a genetics repository, and a data set archive. The three repositories have been funded since June 2003, and Rasooly said the NIDDK’s focus will remain on raising investigator awareness of the rich samples and data sets available.

“The momentum has built up enormously,” she said, noting that scientists have a “passionate” interest in information about some of the NIDDK’s better-known trials. Now the objective is ensuring that the scientific community is aware of the breadth of the samples. “The biggest challenge is to get people to start using the archival samples, especially the archival data sets.”

In the future, the NIDDK plans to continue building efforts by adding studies to those that already provide samples and data to the repositories. Rasooly said she hopes the three repositories will be able to provide a broader range of services to investigators. ■



## End-Stage Renal Disease Rate Stabilizing, USRDS Finds

### Promising Trend Likely Due to Better Care of Patients With Kidney Disease

**T**he rate of end-stage renal disease (ESRD) has stabilized for the first time in the 2 decades such records have been kept, a new Government analysis showed, suggesting that improved treatment may have stopped the steady rise in the number of patients with kidney failure.

The findings, which were released in the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) U.S. Renal Data System (USRDS) 2005 Annual Data Report, show that 338 out of every million Americans had kidney failure in 2003, down slightly from the 340 per million figure in 2002. Still, rates have quadrupled since 1980. The positive news about ESRD comes even as the number of patients at risk for chronic kidney disease continues to grow.

#### Improved Treatment

Those with diabetes constitute 44 percent of new cases of kidney failure, and the population of people with diabetes is growing. Research published during the 1990s recommended that doctors use new medications to help control diabetes and its consequences. New data suggest that more and more patients are receiving those drugs, according to Paul Eggers, Ph.D., USRDS project officer at the NIDDK.

“The number of people with diabetes is going up but ESRD has stabilized, which suggests that despite the increasing epidemic of diabetes, efficacious treatment is available,” Eggers said. Use of heart drugs, such as angiotension-converting enzyme, or ACE, inhibitors and angiotension receptor blockers, or ARBs, protects the kidneys of patients with diabetes. Increasing the use of those medications as treatments is a major goal of the NIDDK’s National Kidney Disease Education Program.



To better understand the reasons for the falling rates of renal failure among people with diabetes, Eggers said the NIDDK is trying to track people with diabetes through the course of their disease to assess whether keeping close track of blood glucose levels is associated with a drop in the risk of kidney failure.

The promising results were not distributed evenly across the patients surveyed, however. The most marked ESRD decrease was in Caucasian people with diabetes who are younger than 40; their rate of kidney failure dropped 47 percent. Other patient groups, particularly African Americans, have not seen similar gains.

Eggers said the USRDS data, though clearly showing disparity, do not pinpoint the underlying reasons. “The fact of the matter is that minority populations, mostly African Americans, but also Native Americans and even Asian Americans, have much higher rates of ESRD.” ■

## Weight Loss Improves Bladder Control in Women With Pre-diabetes

Losing weight not only helps women with pre-diabetes stave off type 2 diabetes, it also improves bladder control, according to study results from the Diabetes Prevention Program (DPP), a landmark clinical study funded by the National Institutes of Health.



Overweight women and women with type 2 diabetes have a 50 to 70 percent increased risk of incontinence.

The DPP randomly assigned 660 women with pre-diabetes to intensive lifestyle changes—stepped-up physical activity and dietary improvements—636 to metformin treatment, and 661 to a placebo. Women in the first group, who made the lifestyle changes and lost 5 to 7 percent of their body weight, had fewer episodes of weekly incontinence than those taking metformin or a placebo. While the weight loss reduced stress incontinence—urine leakage triggered by coughing, sneezing, or exercising—it failed to relieve urge incontinence—unexpected urine leakage.

Overweight women and women with type 2 diabetes have a 50 to 70 percent increased risk of incontinence. One in three women with diabetes or pre-diabetes reports having urinary incontinence once a week or more. For information about NIDDK-funded research on urinary incontinence, visit [www.uitn.net](http://www.uitn.net). For more data from the DPP, which found that losing weight through diet and exercise could reduce the onset of type 2 diabetes by 58 percent, go to [www.niddkrepository.org](http://www.niddkrepository.org). Visit [www.kidney.niddk.nih.gov](http://www.kidney.niddk.nih.gov) to read or download a copy of the NIDDK's fact sheets on urinary incontinence. ■

## High BMI Increases Diabetes Risk for Many Americans

Research by the Centers for Disease Control and Prevention (CDC) assessing the impact of body mass index (BMI) on diabetes risk found that average Americans have a substantial probability of developing diabetes during their lifetime.

The average lifetime risk for diabetes is 20 percent for a normal-weight, 18-year-old man, increasing to 30 percent for overweight men, 57 percent for obese men, and 70 percent for very obese men, according to K.M. Venkat Narayan, M.D., chief of the CDC's Epidemiology and Statistics Branch, Division of Diabetes Translation. Narayan presented the research at the American Diabetes Association's Scientific Sessions in Washington, D.C., in June.

For normal-weight, 18-year-old women, the average lifetime risk is 17 percent, increasing to 35 percent for overweight women, 55 percent for obese women, and 74 percent for very obese women.

A BMI between 20 and 25 is normal; obese people have a BMI of 30 or higher. Nearly two-thirds of U.S. adults are overweight, and nearly one-third are obese.

Narayan and colleagues recently projected that 48.3 million people will be diagnosed with diabetes in the United States by 2050. Their estimate represents a 198 percent increase from 2005, when the number of people with diagnosed diabetes was 16.2 million.

Other CDC research found that people with pre-diabetes have a significantly higher prevalence of hypertension, abnormal lipid levels, and other markers for cardiovascular disease. ■

## NIDDK Chiefs Receive Public Recognition

Four leaders at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) have been publicly recognized for their professional achievements.

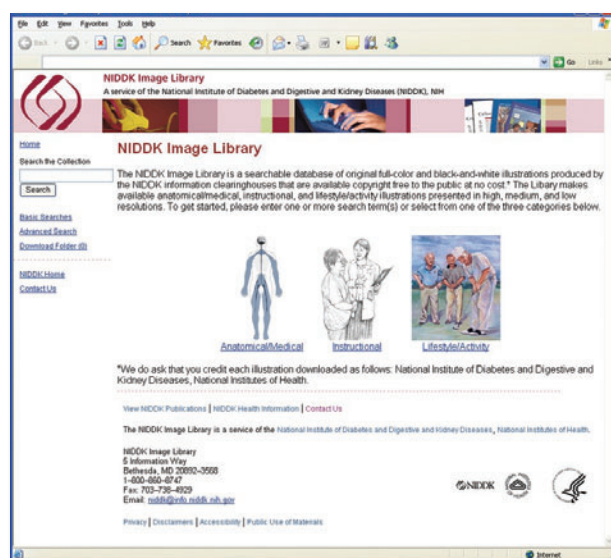
- **William A. Eaton, M.D., Ph.D.**, chief of the laboratory of chemical physics in the NIDDK Division of Intramural Research, was named to the National Academy of Sciences for his distinguished and continuing achievements in original research focusing on fundamental aspects of the protein folding mechanism.
- **Van S. Hubbard, M.D., Ph.D.**, director of the Division of Nutrition Research Coordination and the NIDDK's associate director for nutritional sciences, was promoted to rear admiral in the U.S. Public Health Service.
- **Captain David M. Harlan, M.D.**, chief of the NIDDK's diabetes branch, received the Public Health Service's Research Physician of the Year Award for his research into the pathogenesis and treatment of diabetes.
- **Robert Star, M.D.**, senior scientific adviser for translational biology and acting director of the Division of Kidney, Urologic, and Hematologic Diseases, was recognized for his leadership in developing and overseeing programs to enhance the clinical research workforce for the National Institutes of Health. ■

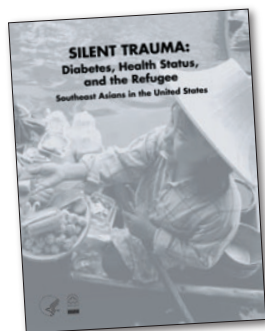
## NIDDK Image Library Goes Live

Need a good picture of a pancreas for your next PowerPoint presentation?

Now you can easily find and access illustrations featured in publications from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

Health care professionals, the general public—anyone—can directly download original, full-color, and black-and-white instructional, anatomical/medical, and lifestyle/activity illustrations produced by the National Diabetes Information Clearinghouse and other NIDDK information clearinghouses. The images are free but the NIDDK should be acknowledged as the source. ■





## NDEP Monograph Examines Diabetes Among Southeast Asian Americans

Although type 2 diabetes is a serious health condition among Southeast Asian Americans, treatment is often complicated by cultural differences and misunderstandings, coexisting health conditions such as depression and anxiety, and lack of health insurance. Unique health care needs among the refugee population and possible under-recognition of diabetes risk by providers and individuals contribute to poor health outcomes.

The National Diabetes Education Program (NDEP) developed a monograph to provide health care providers, policy makers, and other health care professionals successful program models and information to help identify and treat Southeast Asian Americans with diabetes. The monograph also discusses an NDEP subcommittee's recommendations to create collaborative health initiatives, gather baseline diabetes data for program planning, and address the relationship between mental health and diabetes in this population.

For a free copy of the monograph and CD-ROM *Silent Trauma: Diabetes, Health Status, and the Refugee—Southeast Asians in the United States*, visit [www.ndep.nih.gov](http://www.ndep.nih.gov) or call 1-800-438-5383.

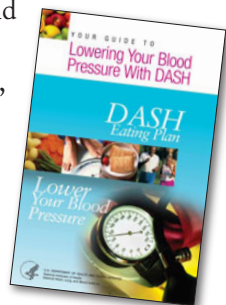
## Your Guide to Lowering Your Blood Pressure With DASH

Updated information about how to lower your blood pressure with the proper diet is now available from the National Heart, Lung, and Blood Institute (NHLBI).

DASH, or Dietary Approaches to Stop Hypertension, developed by the NHLBI, follows heart-healthy guidelines to limit salt, saturated fat, trans fat, and cholesterol, and emphasizes eating more fruits, vegetables, and fat-free or low-fat milk products. The diet is also rich in whole grains, fish, poultry, and nuts.

*Your Guide to Lowering Your Blood Pressure With DASH* incorporates the 2005 U.S. Dietary Guidelines for Americans and includes new information about potassium, weight loss, physical activity, easy-to-prepare recipes, a week's worth of menus, and a food diary to record what you eat and your physical activity level. The guide also offers tips for starting the diet, making heart-healthy choices at every meal, and increasing physical activity.

To order the guide, or to download or view the document online, please visit [www.nhlbi.nih.gov/health/public/heart/hbp/dash](http://www.nhlbi.nih.gov/health/public/heart/hbp/dash). To access the 2005 dietary guidelines, visit [www.healthierus.gov/dietaryguidelines](http://www.healthierus.gov/dietaryguidelines). ■



## NDIC Publication Receives National Awards

The National Diabetes Information Clearinghouse (NDIC) received two national awards for its consumer publication *Your Guide to Diabetes: Type 1 and Type 2*.

The National Institutes of Health (NIH) recognized the publication with its Plain Language Award for excellence. The NIH created the Plain Language Awards to promote the NIH Plain Language Initiative, established in response to a 1998 White House memorandum calling for all Federal Government writing to be in plain, or easy-to-read, format.

The publication also was recognized with a merit award for patient education information from the National Health Information Awards Program. These awards, organized by the Health Information Resource Center, are designed to establish a seal of quality for consumer health information. Health information experts who served as judges considered more than 1,000 entries from hundreds of organizations. ■

